

REFERENCES

- Gill C, Mestril R, Samali A. Losing heart: the role of apoptosis in heart disease. A novel therapeutic target? *FASEB J* 2002;**16**:135–46.
- Gustafsson AB, Gottlieb RA. Mechanisms of apoptosis in the heart. *J Clin Immunol* 2003;**23**:447–59.
- Hynes RO. Integrins: versatility, modulation, and signaling in cell adhesion. *Cell* 1992;**69**:11–25.
- Stupack DG, Cheresch DA. Get a ligand, get a life: integrins, signaling and cell survival. *J Cell Sci* 2002;**115**:3729–38.
- Ross RS. Molecular and mechanical synergy: cross-talk between integrins and growth factor receptors. *Cardiovasc Res* 2004;**63**:381–90.
- Zhidkova NI, Belkin AM, Mayne R. Novel isoform of beta 1 integrin expressed in skeletal and cardiac muscle. *Biochem Biophys Res Commun* 1995;**214**:279–85.
- Simpson DG, Majeski M, Borg TK, et al. Regulation of cardiac myocyte protein turnover and myofibrillar structure in vitro by specific directions of stretch. *Circ Res* 1999;**85**:e59–69.
- Sun M, Opavsky MA, Stewart DJ, et al. Temporal response and localization of integrins beta1 and beta3 in the heart after myocardial infarction: regulation by cytokines. *Circulation* 2003;**107**:1046–52.
- Keller RS, Shai SY, Babbitt CJ, et al. Disruption of integrin function in the murine myocardium leads to perinatal lethality, fibrosis, and abnormal cardiac performance. *Am J Pathol* 2001;**158**:1079–90.
- Shai SY, Harpf AE, Babbitt CJ, et al. Cardiac myocyte-specific excision of the beta1 integrin gene results in myocardial fibrosis and cardiac failure. *Circ Res* 2002;**90**:458–64.
- Communal C, Singh M, Menon B, et al. Beta1 integrins expression in adult rat ventricular myocytes and its role in the regulation of beta-adrenergic receptor-stimulated apoptosis. *J Cell Biochem* 2003;**89**:381–8.
- Stephens LE, Sutherland AE, Klimanskaya IV, et al. Deletion of beta 1 integrins in mice results in inner cell mass failure and peri-implantation lethality. *Genes Dev* 1995;**9**:1883–95.
- Trueblood NA, Xie Z, Communal C, et al. Exaggerated left ventricular dilation and reduced collagen deposition after myocardial infarction in mice lacking osteopontin. *Circ Res* 2001;**88**:1080–7.
- Finsen AV, Christensen G, Sjaastad I. Echocardiographic parameters discriminating myocardial infarction with pulmonary congestion from myocardial infarction without congestion in the mouse. *J Appl Physiol* 2005;**98**:680–9.
- Pfeffer MA, Pfeffer JM, Fishbein MC, et al. Myocardial infarct size and ventricular function in rats. *Circ Res* 1979;**44**:503–12.
- Sumida T, Otani H, Kyoi S, et al. Temporary blockade of contractility during reperfusion elicits a cardioprotective effect of the p38 MAP kinase inhibitor SB-203580. *Am J Physiol Heart Circ Physiol* 2005;**288**:H2726–34.
- Bodeau AL, Berrier AL, Mastrangelo AM, et al. A functional comparison of mutations in integrin beta cytoplasmic domains: effects on the regulation of tyrosine phosphorylation, cell spreading, cell attachment and beta1 integrin conformation. *J Cell Sci* 2001;**114**:2795–807.
- Fassler R, Rohwedel J, Maltsev V, et al. Differentiation and integrity of cardiac muscle cells are impaired in the absence of β1 integrin. *J Cell Sci* 1996;**109**:2989–99.
- Gardin JM, Siri FM, Kitsis RN et al. Echocardiographic assessment of left ventricular mass and systolic function in mice. *Circ Res* 1995;**76**:907–14.
- Yang XP, Liu YH, Rhaleb NE, et al. Echocardiographic assessment of cardiac function in conscious and anesthetized mice. *Am J Physiol Heart Circ Physiol* 1999;**277**:H1967–74.
- Collins KA, Korcarz CE, Lang RM. Use of echocardiography for the phenotypic assessment of genetically altered mice. *Physiol Genomics* 2003;**13**:227–39.
- Anversa P, Li P, Zhang X. Ischemic myocardial injury and ventricular remodeling. *Cardiovasc Res* 1993;**27**:145–57.
- Brancaccio M, Fratta L, Nolte A, et al. Melusin, a muscle-specific integrin beta1-interacting protein, is required to prevent cardiac failure in response to chronic pressure overload. *Nat Med* 2003;**9**:68–75.
- Ingber D. Integrins as mechanochemical transducers. *Curr Opin Cell Biol* 1991;**3**:841–8.
- Nebe B, Rychly J, Knopp A, et al. Mechanical induction of beta 1-integrin-mediated calcium signaling in a hepatocyte cell line. *Exp Cell Res* 1995;**218**:479–84.
- Li Q, Li B, Wang X, et al. Overexpression of insulin-like growth factor-1 in mice protects from myocyte death after infarction, attenuating ventricular dilation, wall stress, and cardiac hypertrophy. *J Clin Invest* 1997;**100**:1991–9.
- Bialik S, Geenen DL, Sasson IE, et al. Myocyte apoptosis during acute myocardial infarction in the mouse localizes to hypoxic regions but occurs independently of p53. *J Clin Invest* 1997;**100**:1363–72.
- Kajstura J, Cheng W, Reiss K, et al. Apoptotic and necrotic myocyte cell deaths are independent contributing variables of infarct size in rats. *Lab Invest* 1996;**74**:86–107.
- Michel JB. Anoikis in the cardiovascular system: known and unknown extracellular mediators. *Arterioscler Thromb Vasc Biol* 2003;**23**:2146–54.
- Frisch SM, Ruoslahti E. Integrins and anoikis. *Curr Opin Cell Biol* 1997;**9**:701–6.

FROM BMJ JOURNALS

Skinfold thickness, body mass index, and fatal coronary heart disease: 30 year follow up of the Northwick Park heart study

Joseph Kim, Tom Meade, Andy Haines

Please visit the Heart website [www.heartjnl.com] for a link to the full text of this article.

Study objective: To examine the effect of baseline body mass index (BMI) and skinfold thickness (ST) on fatal coronary heart disease (CHD) and all cause mortality after 30 years of follow up.

Design: Prospective cohort study.

Setting: Northwick Park heart study (NPHS) designed to investigate the role of haemostatic variables on CHD.

Participants: 1511 men and 691 women enrolled in NPHS aged 40 to 64 years at entry.

Main results: Baseline BMI (kg/m²) and forearm, triceps, subscapular, and suprailiac skinfolds ST (mm) were measured. Cox regression was used to calculate hazard ratios for fatal CHD and total mortality for each standard deviation unit increase in obesity adjusting for age, smoking status, total cholesterol, systolic blood pressure, fibrinogen, and factor VII activity. Subjects experienced 250 fatal CHDs and 819 all cause deaths over 30 years (median: 26 years; IQR: 22–28 years). Among men, only BMI (RR = 1.29, 95%CI = 1.12 to 1.49) significantly increased the risk of fatal CHD. Among women, BMI (RR = 1.48, 95%CI = 1.07 to 2.06), as well as, subscapular (RR = 1.65, 95%CI = 1.19 to 2.30), forearm (RR = 1.46, 95%CI = 1.08 to 1.97), and triceps (RR = 1.63, 95%CI = 1.12 to 2.39) skinfolds were predictive of fatal CHD. None of the estimates for all cause mortality were significant except for subscapular skinfold in women (RR = 1.20, 95%CI = 1.02 to 1.42). There was no evidence of interaction between obesity and sex for fatal CHD or all cause death. The effect of obesity on fatal CHD or all cause deaths does not seem to be mediated substantially by cholesterol, systolic blood pressure, or haemostatic variables.

Conclusions: BMI is an important risk factor for fatal CHD where its prognostic significance remains after up to 30 years of follow up.

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